Real Life Long-Term Survival Analysis in Patients with Chronic Myeloid Leukemia Treated with Tkis in Spain

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Luis Felipe Casado Montero, Valentin Garcia Gutierrez, MD, Pilar Giraldo, MD PhD, Manuel Perez-Encinas, Raquel de Paz, Joaquin Martinez-Lopez, Guiomar Bautista, Santiago Osorio, Maria Jose Requena, Luis Palomera, MD PhD, Maria Jesús Peñarrubia, Carmen Calle, Jose Angel Hernandez-Rivas, Nuria García-Ormeña, Juan Luis Steegmann, MD PhD. ***Blood*** **(2016) 128 (22): 3074. https://doi.org/10.1182/blood.V128.22.3074.3074**

Abstract

Introduction: TKIs introduction in the treatment of chronic myeloid leukemia (CML) has offered an outstanding improvement in prognosis, especially in survival. Data about TKIs were obtained from clinical trials but little is known about their translation to real life. In addition, clinical trials are mainly based on efficacy analysis to just one line of therapy, rather than treatment sequences (due to failure or intolerance).

Objectives: To analyze the long-term survival of patients outside clinical trials in response to TKI treatment, describing the pattern of sequential treatments the patients actually received.

Patients and methods: CML patients in first chronic phase, treated with TKIs (imatinib, nilotinib, dasatinib) either as monotherapy or in sequence, outside clinical trials. The setting was a multicentric, hospital-based registry. Survival and their potentially associated variables were studied.

Results: Demographics, risk and treatment distribution: 696 patients (423 men, 273 women) with a median age at diagnosis of 41y (14-94y) were included with a follow up of 85±7 months (m) from diagnosis, 78±6.6 m from first treatment, and 69±6 m from first TKIs; 106 patients (15%) were over 70y. The risk distributions were as follows: Sokal: low (L) 48%, intermediate (I) 38% and high (H) 13%; Euro score: L 51%, I 45% and H 4%; EUTOS L: 91% and H 9%; EUTOS LT: L 68%, I 25% and H 7%. Treatment groups were the following: Group 1: IFN alpha and then imatinib or 2¼ GTKIs (176 patients); Group 2: imatinib only (340 patients); Group 3: imatinib and then nilotinib, dasatinib or both due to failure or intolerance (131 patients) and Group 4: 2¼GTKIs in first line (49 patients).

Survival: Estimated survival by 10 years was 80%. Ninety-one patients have died (27 due to unknown reasons, 33 due to progression or BMT, 7 due to second neoplasias and 21 due to cardiac or neurological disease).

Variables associated with survival: In the univariate survival analyses (log rank test) either from diagnosis, first therapy or first TKIs, the Sokal, Eutos, Euro and EUTOS LT scores as well as age over 70y were the only statistically significant variables associated

with survival.(figure 1). In the multivariate analysis (Cox model), only Sokal and Eutos LT scores, and age over 70y were independent variables. Patients older than 70 years at diagnosis had a 50% probability of survival by 8 years. It is worth mentioning that, although the probability of overall survival from diagnosis was higher in the group receiving imatinib after IFN alpha, this difference was not seen when measuring the probability of survival after the first treatment o first TKI. This is probably explained by the higher proportion of low-risk score in patients having had previous IFN.

Whereas the cause of death was progression in half of the patients aged equal or less than 70 years, in patients older than 70 years, two third of the deaths were not related to progression of CML.

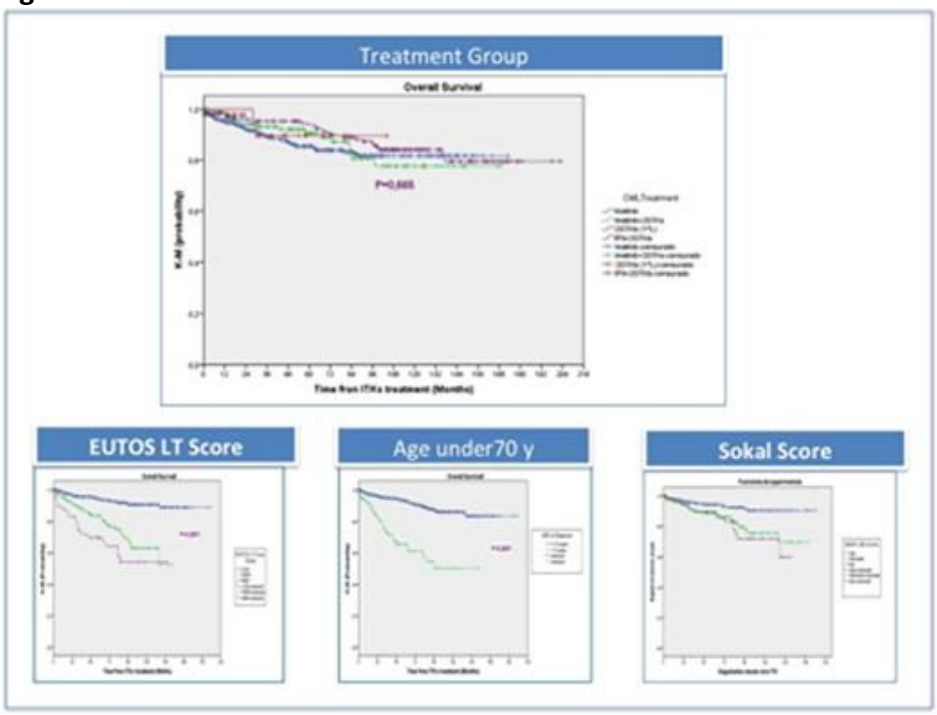
Conclusions:

1.These results show that the probability of survival by 10 years is roughly 80%, and extend the findings of our previous work showing that this probability is not different across different sequential treatments (imatinib before IFN, alone or switched to 2»GTKis due to intolerance o failure)(1). This fact emphasizes the rescue potential of available TKI therapies.

2. We have validated for the first time the Eutos LT score in real life population.

3. Patients over 70 years have shorter survival due to reasons different than progression, opening an interesting field of research, and a non-negligible room of improvement.

Figure 1



(1)Casado LF, et al Cancer Med. 2015 Mar 10.

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Topics: leukemia, myelocytic, chronic, protein-tyrosine kinase inhibitor, spain, imatinib mesylate, cancer, dasatinib,interferon-alpha, nilotinib, sequential treatment, european system for cardiac operative risk evaluation

Author notes: *Asterisk with author names denotes non-ASH members. This icon denotes a clinically relevant abstract